REMARKS

Claims 1-17 are rejected. Claims 18 and 19 are withdrawn from consideration. Claim 1 has been amended. Claims 1-19 are presently pending in the application. Favorable reconsideration of the application in view of the following remarks is respectfully requested.

The basis for the amendment of claim 1 is found on pg. 11, line 29 – pg. 12, line 1 ("*It is preferred that a latent colorant be colorless and not fluoresce.*") and pg. 12, lines 8-11 ("*It is preferred that a latent colorant is colorless and does not have fluorescence.*"), as well as pg. 5, lines 12-13 ("*latent colorants, which are colorless and relatively non-emissive until switched to a colored state*") of the specification as originally filed.

Claim Objections:

The Examiner has objected to Claim 1 because of the limitation "color" recited in line 4 of the claim should be changed to "colorant". Although the Applicants have amended the claim to clarify the meaning, the Applicants do not agree. The previous wording was "wherein said microspheres comprise at least one material with a non-fluorescent latent color that can be developed and used to identify said microsphere". In other words, the microspheres were made of or contained material of a latent color, that could be developed. Replacing "color" with "colorant" would read "at least one material with a non-fluorescent latent colorant that can be developed and used to identify said microsphere". The "material" does not have a latent colorant, but a latent color.

Rejection of Claims 1-5, 7-12, 14-17 Under 35 U.S.C. §102(e):

The Examiner has rejected Claims 1-5, 7-12, 14-17 under 35 U.S.C. 102(e) as being anticipated by Chee et al. (US 6,429,027 B1), indicating that Chee et al. disclose a two-dimensional array of microspheres randomly immobilized in wells of a substrate, wherein the concentration of the microspheres can range from a single microsphere to 2 billion microspheres per cm2, the size of the microspheres can range between 0.2 to 200 microns, the microspheres bear biological probes in the form of a bioactive agent, that binds an analyte of interest, the microspheres can comprise a dye in the form of chromophores that can be developed to produce a unique optical signature that allows one to visually identify the microspheres and the bioactive agent bound to

the microspheres, the chromophores as defined by the Specification absorb light and convert the absorbed light into heat, which is a photo initiated process.

Chee discloses sensor compositions comprising a composite array of individual arrays, to allow for simultaneous processing of a number of samples. Comprising a substrate with a surface having a plurality of assay locations, each assay location comprising an array location, said array location comprising a plurality of discrete sites; and a population of microspheres comprising at least a first and a second subpopulation, wherein said first subpopulation comprises a first bioactive agent and wherein said second subpopulation comprises a second bioactive agent; wherein said microspheres are distributed in said discrete sites in said array location.

The present invention relates to a microarray comprising a support, on which is disposed a layer of microspheres bearing biological probes, wherein the microspheres comprise at least one material with a non-fluorescent latent color that can be developed and used to identify the microsphere.

A claim is anticipated under 102(e) only if each and every element as set forth in the claim is found, either expressly or inherently, in a single prior art reference. Verdegaal Bros. V. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Chee describes a "a molecule whose color or luminescence properties change in the presence of a selectively-binding DBL."(col. 15, lines 36-38), "a molecule whose color or luminescence properties change in the presence of various solvents." (col. 15, lines 43-46), "a derivative of fluorescein whose color changes between aqueous and nonpolar solvents." (col. 15, lines 48-50), and "In general, labels fall into three classes: a) isotopic labels, which may be radioactive or heavy isotopes; b) magnetic, electrical, thermal; and c) colored or luminescent dyes; although labels include enzymes and particles such as magnetic particles as well." (col. 19, lines 33-37). Chee describes a colored molecule that changes to a different color or fluoresces. Chee fails to disclose a colorless and non-fluorescent molecule as presently claimed. Therefore, Chee fails to anticipate the present claims.

Rejection Of Claim 6 Under 35 U.S.C. §103(a):

The Examiner has rejected Claim 6 under 35 U.S.C. 103(a) as being unpatentable over Chee et al. in view of Zuk et al. (US 4,256,834), as Chee

et al. disclose the microarray recited in claim 6 except that the reference does not disclose that the optical signature is developed by the means recited in the claim, but Zuk et al. disclose an immunoassay comprising the use of a chemiluminescer that undergoes an enzyme catalyzed redox reaction to produce a detectable signal, making it obvious to utilize a chemiluminescer disclosed by Zuk et al. as the optical signature means for the microspheres disclosed by Chee et al. as the use of such chemiluminescers would be beneficial in assays in which the assay conditions favor chemiluminescence over fluorescence.

Chee discloses sensor compositions comprising a composite array of individual arrays, to allow for simultaneous processing of a number of samples. Comprising a substrate with a surface having a plurality of assay locations, each assay location comprising an array location, said array location comprising a plurality of discrete sites; and a population of microspheres comprising at least a first and a second subpopulation, wherein said first subpopulation comprises a first bioactive agent and wherein said second subpopulation comprises a second bioactive agent; wherein said microspheres are distributed in said discrete sites in said array location.

Zuk discloses novel immunoassays employing discrete particulate reagents for determining an analyte which is a member of a specific binding pair-ligand and homologous receptor. The assay employs as a first reagent, a member of a pair bound to an insoluble particle (particle conjugate); as a second reagent, a label which is part of a signal producing system, bound to a member of the pair (signal label conjugate); and as a third reagent, a signal repressor comprising an insoluble particle, where the signal repressor is obstructed from interacting with the label of the signal label conjugate, when the signal label conjugate is bound to the particle conjugate. In performing the assay, the analyte, the reagents, and any ancillary materials are combined in an aqueous assay medium and the signal determined as compared to an assay medium having a known amount of analyte. The repressor greatly enhances the sensitivity and accuracy of the immunoassay in repressing the signal produced by labels which are not bound to the particle conjugate, thus substantially limiting the observed signal to label bound to the particle conjugate. The labels which are employed provide a signal which does not differ significantly from when the signal label conjugate is bound to the particle conjugate or is free in the bulk solution. Illustrative labels include

chromogens, such as fluorescers, chemiluminescers, and the like. Particular reagents and kits are provided, where the kits have predetermined amounts of the various reagents to substantially optimize the sensitivity of the assay.

The present invention relates to a microarray comprising a support, on which is disposed a layer of microspheres bearing biological probes, wherein the microspheres comprise at least one material with a colorless and non-fluorescent latent colorant that can be developed to a color and be used to identify the microsphere.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the reference or in the general knowledge available to one skilled in the art to modify the reference, there must be a reasonable expectation of success, and the prior art reference must teach or suggest all the claim limitations.

Claim 6 benefits from dependence on claim 1, which, as discussed above, Applicants believe is inventive even in light of Chee. Chee describes a colored molecule that changes to a different color or fluoresces. Chee fails to disclose a latent colorant, that is, a molecule which "is colorless and does not have fluorescence", as defined in the present specification. Zuk also fails to disclose a colorless, latent, non-fluorescent colorant as presently claimed. As neither reference suggests the use of a color-free material that can be switched on to form a colored material, especially a non-fluorescing compound, the references fail to provide any suggestion to modify to produce the presently claimed invention.

There is also no likelihood of success provided in the references. There is no suggestion to use a non-fluorescing, colorless colorant, which can be developed to form a colored material. The present invention deals with the problem of background noise caused by fluorescence, which lowers or interferes with the detectability of a material producing an optical signal. (pg. 5, line 10). The references fail to deal with this problem, preferring instead to actually use fluorescent materials.

Neither Chee nor Zuk disclose the use of a latent colorant, a developable latent colorant or a non-fluorescing latent colorant as presently claimed.

The present invention also provides a surprising improvement. The present invention provides improved signal detectability, by providing a

latent colorant, which would have no signal, and converting it to a colorant, which would have a detectable signal. The detectability is improved, as detection relates to an "on" / "off" or signal / no signal detection scenario, as opposed to a detection system aimed at detecting a shift in a signal, as taught by Chee, col. 21, line 21 ("*leading to differences in signal intensity*"). In other words, the present invention relies on the fact that it is easier to detect a color compared to an absence of color, as opposed to a shift in color.

Since Chee and Zuk, alone or in combination, fail to suggest the modification necessary to produce the present claims, fail to provide any likelihood of success and fail to disclose all of the present claim limitations, the Applicants request that the Examiner reconsider and withdraw the rejection.

Rejection Of Claim 13 Under 35 U.S.C. §103(a):

The Examiner has rejected Claim 13 under 35 U.S.C. 103(a) as being unpatentable over Chee et al. in view of Wang (US 4,663,277), as Chee et al. disclose the microarray of claim 13 except for the recital of the immobilization of the microspheres by a gelation process, but Wang discloses an immunoassay for a virus accomplished by utilizing microspheres coated with antiviral antibodies and discloses that the method of the immunoassay involves immobilizing the microspheres by placing the microspheres in a gel, making it obvious to one of ordinary skill in the art to further immobilize the microspheres disclosed by Chee et al. by means of a gel as taught by Wang so that

Claim 13 benefits from dependence on claim 1, which, as discussed above, Applicants believe is inventive even in light of Chee. Chee discloses sensor compositions comprising a composite array of individual arrays, to allow for simultaneous processing of a number of samples. Comprising a substrate with a surface having a plurality of assay locations, each assay location comprising an array location, said array location comprising a plurality of discrete sites; and a population of microspheres comprising at least a first and a second subpopulation, wherein said first subpopulation comprises a first bioactive agent and wherein said second subpopulation comprises a second bioactive agent; wherein said microspheres are distributed in said discrete sites in said array location.

Wang relates to the detection and/or the determination of viruses by an immunoassay method, to materials for such method, and to a virus detection

kit. Viruses are detected by means of an immunoassay method in which an extended solid phase coated with antiviral antibody is employed to bind and remove virions from a specimen by forming an immuno-complex with antigens of the virions, a mobile solid phase comprising a dispersion of microspheres coated with the antiviral antibody is used to bind the microspheres to antigens associated with the immuno-complex, and the presence of bound microspheres is detected. The detection sensitivity is amplified by the ability to more readily detect the microspheres, which may be dyed or labeled. The extended solid phase advantageously may be in the form of a dipstick which can be easily contacted with the specimen. A virus detection kit provides the extended solid phase and mobile solid phases, each coated with antiviral antibodies.

The present invention relates to a microarray comprising a support, on which is disposed a layer of microspheres bearing biological probes, wherein the microspheres comprise at least one material with a non-fluorescent latent color that can be developed and used to identify the microsphere.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the reference or in the general knowledge available to one skilled in the art to modify the reference, there must be a reasonable expectation of success, and the prior art reference must teach or suggest all the claim limitations.

Chee describes a colored molecule that changes to a different color or fluoresces. Chee fails to disclose a latent colorant, that is, a molecule which "is colorless and does not have fluorescence", as defined in the present specification. Wang also fails to disclose a latent, non-fluorescent colorant as presently claimed. As neither reference suggests the use of a color-free material that can be switched on to form a colored material, especially a non-fluorescing compound, the references fail to provide any suggestion to modify to produce the presently claimed invention.

There is also no likelihood of success provided in the references. There is no suggestion to use a non-fluorescing, colorless colorant which can be developed to form a colored material. The present invention deals with the problem of background noise caused by fluorescence, which lowers or interferes with the detectability of a material producing an optical signal. (pg. 5, line 10).

The references fail to deal with this problem, preferring instead to actually use fluorescent materials.

Neither Chee nor Wang disclose the use of a latent colorant, a developable latent colorant or a non-fluorescing latent colorant as presently claimed.

The present invention also provides a surprising improvement. The present invention provides improved signal detectability, by providing a latent colorant, which would have no signal, and converting it to a colorant, which would have a detectable signal. The detectability is improved, as detection relates to an "on" / "off" or signal / no signal detection scenario, as opposed to a detection system aimed at detecting a shift in a signal. In other words, the present invention relies on the fact that it is easier to detect a color compared to an absence of color, as opposed to a shift in color.

Since Chee and Wang, alone or in combination, fail to suggest the modification necessary to produce the present claims, fail to provide any likelihood of success and fail to disclose all of the present claim limitations, the Applicants request that the Examiner reconsider and withdraw the rejection.

Prior Art:

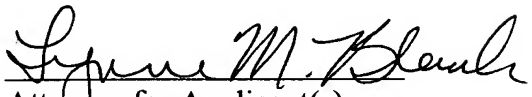
The Examiner notes Walt et al. (US 6,023,540) as prior art made of record and not relied upon is considered pertinent to applicants' disclosure, which disclose a two-dimensional array of microspheres immobilized in wells disposed at the end of an optical fiber, the microspheres comprise biological probes in the form of functional groups, and a plurality of dyes in varying ratios that define an optical signature for each type of microsphere and analyte, the dyes display a change in its optical signature once an analyte exclusively interacts with the functional groups disposed on the surface of the microspheres, which enables one to identify the microsphere and the analyte.

Walt et al. (US 6,023,540) disclose a two-dimensional array of microspheres immobilized in wells disposed at the end of an optical fiber. The microspheres comprise biological probes in the form of functional groups, and a plurality of dyes in varying ratios that define an optical signature for each type of microsphere and ana4yte. The dyes display a change in its optical signature once an analyte exclusively interacts with the functional groups disposed on the surface of the microspheres, which enables one to identify the microsphere and the

analyte. However, Walt fails to mention the use of a colorless and non-fluorescent, developable, latent colorant.

It is believed that the foregoing is a complete response to the Office Action and that the claims are in condition for allowance. Applicants respectfully request that this amendment be admitted in order to present the rejected claims in better form for consideration on appeal.

Respectfully submitted,



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